

16 FEB 2005

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
26 February 2004 (26.02.2004)

PCT

(10) International Publication Number
WO 2004/016586 A2

(51) International Patent Classification⁷: **C07D**

Galveston, TX 77550 (US). **HOLBROOK, Michael**
[—US]; 1611 Norwood Pl., Oklahoma City, OK 73120
(US).

(21) International Application Number:
PCT/US2003/025681

(74) Agent: **LANDRUM, Charles, P.**; Fulbright & Jaworski
L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX
78701 (US).

(22) International Filing Date: 18 August 2003 (18.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/403.893 16 August 2002 (16.08.2002) US
60/445.581 6 February 2003 (06.02.2003) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,
SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(63) Related by continuation (CON) or continuation-in-part
(CIP) to earlier applications:

| | |
|----------|------------------------------|
| US | 60/403.893 (CON) |
| Filed on | 16 August 2002 (16.08.2002) |
| US | 60/445.581 (CON) |
| Filed on | 6 February 2003 (06.02.2003) |

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **BOARD
OF REGENTS THE UNIVERSITY OF TEXAS SYS-
TEM** [US/US]; 201 West Seventh Street, Austin, TX
78701 (US).

Published:

— *without international search report and to be republished
upon receipt of that report*

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **BARRETT, Alan**
[GB/US]; 13648 Mutiny Lane, Galveston, TX 77554
(US). **BEASLEY, David** [AU/US]; 102 Albacore Avenue,

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: COMPOSITIONS AND METHODS RELATED TO FLAVIVIRUS ENVELOPE PROTEIN DOMAIN III ANTIGENS

(57) Abstract: The present invention concerns methods and compositions involving flavivirus envelope protein domain III antigens for the detection of virus and detection of antibodies against the virus. Such methods and compositions may be used to detect TBE serocomplex viruses or West Nile virus infection in a subject, patient, animal or biological fluid. The present invention also concerns kits for implementing such methods. In some embodiments, kits contain a recombinant TBE serocomplex virus or West Nile virus envelope protein domain III antigen.

WO 2004/016586 A2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/25681

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53

US CL : 435/7.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/ 184.1, 186.1, 202.1, 204.1, 218.1; 435/5, 7.1, 69.1, 69.3, 70.1; 530/300, 350; 536/27.72

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-------------|--|--|
| X — A | US 6,258,788 (SVHMALJOHN) 10 July 2001 (10.07.2001) especially columns 11-16. | 1, 13, 14, 18-21, 29-33, 36-43 ----- 2-12, 15-17, 23-28, 34-36 |
| X | US 6,165,477 (IVY et al.) 26 December 2000 (26.12.2000) se claims. | 21, 30, 31 |
| X | TRENT et al. Solid-phase radioimmunoassay for antibodies to flavivirus structural and nonstructural proteins. Infection and Immunity, May 1976, Vol. 13, No. 5, pages 1325-1333, see abstract. | 1-4, 18, 21, 30-33, 37, 38, 43 |
| X | KLIMES et al. Prevalence of antibodies to tickborne encephalitis and West Nile flaviviruses and the clinical signs of tickborne encephalitis in dogs in the Czech Republic. Veterinary Record, January 2001, Vol. 148, No. 1, pages 17-20. | 1, 2, 18, 20, 21, 32, 33, 42, 43 |
| X | WANG et al. West Nile virus envelope protein: role in diagnosis and immunity. Annals New York Academy of Science, December 21001, Vol. 951, pages 325-327. | 1-3, 5, 13, 15, 18-21, 28-34; 36-41, 43 |



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

02 August 2004 (02.08.2004)

Date of mailing of the international search report

20 SEP 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 872-9306

Authorized officer

Ulrike Winkler

Telephone No. (571)-272-1600

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| X | WANG et al. Immunization of mice against West Nile virus with recombinant envelope protein. Journal of Immunology, November 2001, Vol. 167, No. 9, pages 5273-5277. | 30, 31 |
| X | HEINZ et al. The flavivirus envelope protein E: isolation of a soluble form from tick-borne encephalitis virus and its crystallization. Journal of Virology, October 1991, Vol. 65, No. 10, pages 5579-5583. | 13 |
| --- | | ----- |
| Y | | 28-31 |
| Y | CRILL et al. Monoclonal antibodies that bind to domain III of dengue virus E glycoprotein are the most efficient blockers of virus adsorption to Vero cells. Journal of Virology, August 2001, Vol. 75, No. 16, pages 7769-7773. | 1, 4, 13, 18, 19 |
| Y | HEINZ et al. Monoclonal antibodies to the structural glycoprotein of tick-borne encephalitis virus. Infection and Immunity, September 1982, Vol. 37, No. 3, pages 869-874. | 32, 33, 36-39, 42, 43 |
| Y | Gaunt et al. Phylogenetic relationships of flaviviruses correlate with their epidemiology, disease association and biogeography. Journal of General Virology, August 2001, Vol. 82, No. 8, pages 1867-1876, see AF372405. | 6-11, 23-27, 35 |
| Y | NI et al. Attenuation of Japanese encephalitis virus by selection of its mouse brain membrane receptor preparation escape variants. Virology, February 1998, Vol. 241, NO. 1, pages 30-66, see AF036915. | 10, 11, 35 |
| Y | KUNO et al. Genomic sequencing of deer tick virus and phylogeny of powassan-related viruses of North America. American Journal of Tropical Medicine and Hygiene, November 2001, Vol. 65, No. 5, pages 671-676, see AF310913. | 10, 11, 35 |

INTERNATIONAL SEARCH REPORT

PCT/US03/25681

Continuation of B. FIELDS SEARCHED Item 3:

WEST, DERWENT, STN-BIOSIS, MEDLINE, EMBASE

SEQ ID NO: 8, 11 and 20, inventor search, ELISA, West Nile, flavivirus, TBE, tick borne encephalitis virus, domain III, E protein, ectodomain.